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09/724,379	11/28/2000	Hong Jin	7682-055-999	9862

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,379	JIN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-18* is/are pending in the application.

4a) Of the above claim(s) *9,11 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/2&22/01, 6/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 7-18 are pending in the application.

2. Applicant's election of Group I (polynucleotides comprising paramyxoviridae genomes modified by insertion of a heterologous sequence), and subgroups A (wherein the virus is RSV) and (s) wherein the heterologous sequence is from another RSV in the reply filed on April 26. 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 9, 11, and 15-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 26, 2004.

4. Currently, claims 7, 8, 10, and 12-14 are under consideration insofar as they read on the elected invention and generic claims thereto.

Priority

5. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date to either U.S. application 08/316,439 under 35 U.S.C. 120 or to U.S. provisional application 60/069,153 under 35 U.S.C. 119(e) as follows: the present application does not share at least one named inventor with those listed in the applications to which priority is claimed. Because the present application does not share priority with either of the indicated

applications, the Applicant has not met the conditions for receiving benefit of the earlier filing dates of these applications.

6. With respect to the provisional application 60/069,153, identified in the first paragraph of the specification as amended on April 26, 2004, it appears that the applicant intended to refer to application 60/060,153 instead.

Information Disclosure Statement

7. The information disclosure statements (IDS) submitted on March 2 and March 22 of 2001, and on June 11 of 2003 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

8. It is noted that only certain pages of the Lodish et al. reference, cited in the June 11, 2003 IDS, were provided. The reference has therefore been considered only to the extent of the pages submitted by the Applicant.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 8, 10, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on polynucleotides comprising an RSV genome or antigenome with an inserted heterologous sequence, wherein the genome or the

inserted sequence comprises sequences "derived from respiratory syncytial virus." It is not clear what is meant by the phrase "derived from." It is unclear if the phrase requires the genome or sequence is isolated from RSV, or if the language indicates that the sequence may vary from an RSV sequence by additional modifications.

Clarification is required.

11. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is rejected for two reasons.

First, there is not antecedent basis in the claims for the language "said nucleotide modification species." It is not clear what the term "species" is referring to.

Second, it is not clear what is meant by the claim language identifying the modification species as an attenuated phenotype. A phenotype is understood in the art to constitute the characteristics displayed by an organism, or its observable characteristics. See e.g., the definitions of "phenotype" by the On-Line Medical Dictionary, and the Science and Biotechnology dictionary. Because a polynucleotide alone does not display the phenotypic traits that it encodes, it is unclear how a polynucleotide alone would have an attenuated phenotype.

It is suggested that the claim be amended such that it describes the polynucleotide of claim 12, wherein the modified genome encodes a virus with an attenuated phenotype.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim describes an isolated polynucleotide comprising a modification to a paramyxovirus genome, wherein the modification results in an attenuated phenotype.

In the application, the Applicant has suggested alterations of the RSV genome that may result in attenuated phenotypes. Additionally, the application suggests the use of multiple forms of scanning or random mutagenesis to identify genetic alterations that result in such attenuation. However, the application does identify all of the potential targets for genetic alteration that would result in attenuated forms of the virus. Thus, in comparison the scope of the claims, the Applicant has provided few, if any, working examples, and little guidance towards other operative embodiments.

Further, not all genetic alterations are likely to result in attenuated virus. The art surrounding the alteration of proteins, which are encoded by viral genes, indicates both that such proteins are tolerant to alteration without loss of function, but that in each protein certain amino acids are tolerant to only a limited type, or to no, alteration without a loss of function. Bowie et al., Science 247: 1306-10, esp. page 1306 right column paragraphs 2 and 3. Bowie also teaches that the effect of any particular mutation is unpredictable absent teachings regarding the association of the residue(s) to be mutated with the protein's structure and function. Id. While the

teachings of Bowie relate to proteins, these teachings would also relate to the modification of genes coding for proteins. Thus, the art indicates that mutation of any particular (one or more) nucleotides in the RSV genome may have no effect, may attenuate or increase the virus' virulence, or may prevent the rescue of a viable virus. Specific modifications to the regulatory domains of the viral genome could also be expected to achieve such varied results. Such expectations are supported by the teachings in the current application. See e.g., pages 58-59, and 62-63 (indicating that modifications to the viral gene encoding the L protein resulted in such varied results, some resulting in no change, some in attenuation, others in an increase in L protein function, and others in rendering a virus not viable). The art therefore teaches that the art surrounding the claimed invention is therefore both largely unpredictable, and complex.

In contrast to these teachings, the present application provides very little in the specific identification of what nucleotides in the viral genome would be likely to achieve which of the potential effects. The Applicant has not provided sufficient detailed teachings of relating specific nucleotides of the genome to viral activities, or which of the nucleotides may be modified to achieve a viable virus with an attenuated phenotype, such that those in the art would be able to make and use attenuated RSV to the extent claimed. It is noted that the Applicant has provided screening methods to help make such determinations. It is also noted that the Applicant has provided information as to certain specific mutations that may be made to the genome that would result in attenuated phenotypes. However, the claims are not limited to such embodiments, and the information disclosed with relation to these specific mutations provides little guidance in comparison to the scope of what is being claimed.

In view of the large size of the viral genome and genetic alterations encompassed by the claims, an thus the number of potential mutations that may be made, the limited specific guidance, and the complexity and unpredictability in the art, the Applicant has not provided sufficient information to enable those in the art to make or use any attenuated RSV.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 7 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoffman et al.(J Virol 71: 4272-77- of record in the March 2, 2001 IDS). The claims read on any isolated polynucleotide molecule comprising a genome or antigenome of a paramyxovirus into which a heterologous sequence has been inserted. The term "heterologous sequence" appears to be used in the application as including any mutation of native viral sequences.

The Hoffman reference teaches the use of a cDNA clone comprising a mutated version of a paramyxovirus virus for the rescue of mutated virus. Pages 4272-73. The reference therefore anticipates that indicated claims.

16. Claims 7 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by the teachings of Park et al., PNAS 88:5537-41 (of record in the March 2 2001 IDS). The claims read on any isolated polynucleotide molecule comprising a genome or antigenome of a paramyxovirus into which a heterologous sequence has been inserted. The term "heterologous sequence" appears to be used in the application as including both insertion of foreign material, or rearrangement or mutation (including addition or deletion) of native viral sequences. Pages 32-33. Thus, the claims read on polynucleotides that comprise deletions of the native viral sequences and insertion of foreign sequences. Such a polynucleotide is disclosed by the teachings of Park. See, pages 5537-38. The reference therefore anticipates the indicated claims.

17. Claims 7, 8, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by either of Collins et al. (PNAS 88: 9663-67) or Collins et al. (Virology 195:252-56). (Both references of record in the March 2, 2001 IDS). The claims have been described above except that the dependent claims further require that the viral genomes be derived from RSV. The Collins references provide teachings similar to those if Park above, except that the paramyxovirus comprising the foreign gene is an RSV. PNAS article, pages 9663-64, and Virology article, generally. The references therefore anticipate the indicated claims.

18. Claims 7, 8, 10, and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by either of Collins (U.S. Patent 6,264,957). These claims read on polynucleotides comprising modified RSV genomes, or modified paramyxovirus genomes comprising a heterologous RSV

sequence. The patent claims such a polynucleotide. See, claims 19-22. The reference therefore anticipates the indicated claims.

It is noted that the cited reference does not pre-date the earliest filed application to which the present application claims benefit. However, as was indicated above, the Applicant has not met the statutory conditions for receiving benefit to the earlier U.S. Application 08/316,439. The Collins patent is therefore considered prior to the application.

19. Claims 7, 8, 10, and 12-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Murphy et al., (U.S. Patent 5,993,824, of record in the IDS of June 11, 2003). The claims have been described in part above. The claims indicate that the modification to the claimed polynucleotide comprises an introduction of a heterologous sequence. The term "heterologous sequence" appears to be used in the application as including both insertion of foreign material, or rearrangement or mutation of native RSV sequences. Pages 32-33. Thus, the claims read on isolated polynucleotides comprising insertions of mutated sequence of the RSV from which the claimed polynucleotide was derived.

The Murphy patent teaches the isolation of clones of the RSV genome, and the insertion into the genome of mutations derived from known attenuated RSV particles. See e.g., columns 80-93. The reference teaches the isolation of the RSV genome, the use of such to make attenuated virus through inserting heterologous sequences. The reference therefore anticipates the indicated claims.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 7, 8, 10, and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clarke et al. (WO 96/10632- of record in the June 11, 2003 IDS). The claims have been described above. This reference teaches the use of isolated polynucleotides comprising RSV genomes for the rescue of modified RSV virus, including embodiments wherein the modification comprised the insertion of a foreign sequence (including from another RSV), and alterations that cause viral attenuation. The currently claimed polynucleotides are therefore obvious over the teachings of the Clarke reference.

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 7 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-41 of copending Application No. 10/371,099, claims 1 and 2 of copending Application No. 10/245,644 . Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending applications represent species of the presently claimed genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

24. Claims 7, 10, 12, and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13, 27, and 28 of copending Application No. 09/161,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending applications represent species of the presently claimed genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claims 7, 10, 12, and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 8, 9, 10, and 11 of copending Application No.10/876,113. Although the conflicting claims are not identical, they are

not patentably distinct from each other because the claims of the copending applications represent species of the presently claimed genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 7, 8, 10, and 12-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 5,840,520. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent cover overlapping subject matter with the present claims. Additionally, the embodiments identified in the claims were described in the portions of the patent specification relating to the claimed RNA molecules. See e.g., columns 43, and 44 (lines 19-42). Thus, the present claims are directed towards embodiments of the invention claimed in the patent, and which were suggested in the specification of that patent.

27. Claims 7, 8, 10, and 12-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 5,166,057. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim of the patent is generic to the claims of the present application. Additionally, while the claims of the copending application do not specifically identify the virus as a paramyxovirus, RSV, or as attenuated, these embodiments of the patent claims are described in the specification of the patent. See, columns 3 (lines 31-37), 15-16 (esp. lines 3-20), 26 (lines

11-38). Thus, the present claims are directed towards embodiments of the invention claimed in the patent, and which were suggested in the specification of that patent.

28. The above rejections are, in part, based on the specification of a previously issued patent, rather than the claims. In support of the use of this material, the examiner notes the following excerpt from MPEP section 804 II(B)(1):

> When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. This does not mean that one is precluded from all use of the patent disclosure.
>
> The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Thus, the courts have held that it is permissible to use the specification in determining what is included in, and obvious from, the invention defined by the claim on which the rejection is based. This is true even where elements are drawn from the specification describing the claimed invention which are not elements in the claim itself.

Conclusion

29. No claims are allowed.

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 10/4/04
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